REMARKS

Enclosed herewith in full compliance with 37 C.F.R. §§1.821-1.825 is a Sequence Listing to be inserted into the specification as indicated above. The Sequence Listing in no way introduces new matter into the specification. Also submitted herewith in full compliance with 37 C.F.R. §§1.821-1.825 is a disk copy of the Sequence Listing. The disk copy of the Sequence Listing, file "1291-0186.ST25.TXT", is identical to the paper copy, except that it lacks formatting.

The specification has been amended to include the SEQ ID NOS where appropriate. No new matter is introduced by these amendments.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,
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MSW/LPS

Attachments:
Disk Copy of Sequence Listing
Paper Copy of Sequence Listing
Copy of Notice
Version with Markings Showing Changes Made

(Rev. 03/27/01)

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

The paragraph beginning on page 13, line 1, has been amended as follows:

-- In one specific and illustrating embodiment, the PNA-NLS complex according to the invention is described by formula III:

GCG CTC GGC CCT TTC **(SEQ ID NO:1)** L Pro Lys Lys Lys Arg Lys Val **(SEQ ID NO:2)** (III),

wherein L is described by formula IV:

$NHCH_2CH_2OCH_2CH_2OCH_2CO_2H$ (IV).

However, as the man skilled in the art will easily realise, variations may be made to these sequences while still providing an advantageous synthetic transport entity within the scope of the present invention as defined by the appended claims. Using the present invention, it is possible to mimic the different functions of viruses and microorganisms by attaching functions directly to a nucleic acid or any other biological molecule and/or complex to be transferred to a cell. At the same time, deleterious properties of native viral vectors are avoided by the use of the present transfer entity.--

The paragraph beginning on page 21, line 28, has been amended as follows:

--The peptide nucleic acid (PNA) was synthesised at Perspective BioSynthesis Ltd. The sequence of the PNA was chosen with the criteria of being excluded from the plasmids as well as from known eucaryotic DNA sequences to avoid possible non-specific binding. The PNA

peptides were attached with the hydrophobic spacer Fmoc-$NC_6O_3H_{11}$-OH (Fmoc-AEEA-OH) to a stretch of amino acid residues, PKKKRKV **(SEQ ID NO:2)**, the SV40 core NLS. The complete sequence is GCGCTCGGCCCTTCC **(SEQ ID NO:3)**-linker-PKKKRKV **(SEQ ID NO:2)**. Like peptides, PNA is synthesized on a polyethylene glycol-polystyren (PEG-PS) support with a peptide amide linker, the linker yielding a PNA amide upon cleavage of the final product (http://www.pbio.com/cat/synth/pna/pnacycle.htm).--

The paragraph beginning on page 26, line 2, has been amended as follows:

--The present invention demonstrates that a PNA molecule linked to an SV40 NLS peptide can work as a nuclear targeting signal when hybridised to a fluorescent labelled oligonucleotide or to a plasmid containing a reporter gene. Similar results were obtained using DOTAP or 25 kD PEI as transfection reagents in HeLa, NIH- 3T3 or COS- 7 cells, demonstrating the versatility of the technique (data not shown). The method according to the invention is of potential value for transfections in general and may also be applied in the context of gene therapy or DNA-vaccination. The increased uptake of nucleic acids into target cells may be vital for gene expression, as well as for the delivery of anti-sense constructs or mutation-inducing oligonucleotides. In the context of anti-sense activity it should also be possible to apply a PNA-NLS construct alone. According to the present invention, a PNA target sequence, CGCGAGCCGGGAAGG **(SEQ ID NO:4)**, was used, which does not exist in the unmodified EGFP or the lacZ plasmids that were studied. The interaction of PNA with its target sequence is highly specific and the PNA does not cross-hybridise to non-related sequences. The strong interaction between DNA and PNA also prevents the compex from dissociating (Knudsen H.,

Nielsen P .E.: Antisense properties of duplex- and triplex-forming PNAs, Nucleic Acids Research 24(3) 494-500 (1996)).--